

Relationship Between Helicobacter Pylori Infection and Gastroesophageal Reflux Disease (GERD)

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ABSTRACT

Introduction: *Helicobacter Pylori* infection is a gastrointestinal infection that affects about 50% of the world's population; however, its prevalence varies across geographic areas. The actual relationship of *H. Pylori* with Gastroesophageal Reflux Disease (GERD) is still unclear because some studies report a high prevalence of *H. Pylori* in GERD patients, but some studies report the opposite. This study aims to determine the relationship between *H. Pylori* infection and GERD and the prevalence of *Helicobacter Pylori* infection in GERD patients at Eka Hospital Pekanbaru.

Methods: This study was a cross-sectional study of GERD patients who had undergone endoscopy at Eka Hospital Pekanbaru from January 2021 to December 2022. There were 219 patients. This research was then analyzed with the Chi-Square Test using SPSS version 22.

Results: A total of 219 GERD patients met the criteria for this study. 108 of them were positive for *H. Pylori* from the results of endoscopic biopsies. The prevalence of GERD patients infected with *H. Pylori* is 49.3%. 108 of them were positive patients, 14 (13%) GERD patients were ≥ 60 years old and < 60 years were 94 (87%). Of the 108 positive patients, 53 (49.1%) were male, 55 (50.9%) female. Where age and gender did not significantly increase the risk of *H. Pylori* infection ($p > 0.05$). The most common endoscopic biopsy finding is chronic erosive gastritis.

Conclusion: Although the prevalence of GERD patients infected with *H. Pylori* was quite large (49.3%), there was no significant association between GERD patients and the incidence of *H. Pylori* infection.

Keywords: *Helicobacter Pylori*, GERD, Gastritis

INTRODUCTION

H. Pylori infection is estimated to affect around 50% of the world's population, however, the prevalence varies across geographic areas(1). *H. Pylori* infection worldwide in 2015 had a prevalence that varied widely depending on the region and country with the highest prevalence in Africa (79.1%), Latin America and the Caribbean (63.4%), and Asia (54.7%)(2). In contrast, the prevalence of *H. Pylori* was lowest in North America (37.1%) and Oceania (24.4%)(3). By the turn of the twenty-first century, the prevalence of *H. Pylori* had declined in the highly industrialized countries of the Western world, whereas the prevalence was higher in developing and newly industrialized countries(3). The prevalence of *H. Pylori* infection in Indonesia is influenced by ethnicity and genetic characteristics, which are crucial factors in determining the rates of

H. Pylori infection rates in Indonesia(4). The Batak, Papuan, and Bugis ethnic groups are more susceptible to infections than the Javanese, the dominant ethnic group(4). In six studies of patient dyspepsia in Indonesia, the prevalence of *H. Pylori* infection varied from 5.7% to 68% and the highest prevalence was found in Jakarta using a rapid urease test, culture and histology(4). It has been discovered that this gram-negative micro-aerobic bacterial infection is responsible for developing peptic ulcer disease, gastric mucosal lymphoma, and gastric cancer(5).

Gastroesophageal reflux disease (GERD) is one of the most common gastroenterological diseases(6). Gastroesophageal reflux disease (GERD) is a common condition in which reflux of gastric contents into the esophagus causes symptoms and/or complications(7). Gastroesophageal Reflux Disease (GERD) has a

complex pathophysiology in the form of a dysfunctional esophagogastric junction, an antireflux barrier consisting of the LES and crural diaphragm, coupled with impaired esophageal clearance and changes in the integrity of the esophageal mucosa(8). Research conducted at Fatmawati Hospital, Jakarta, in 2021 found that the prevalence of GERD was 49%(9). This condition is caused by many factors, namely environmental factors, diet, and physiology(5). The prevalence of GERD in Asian countries such as Iran ranges from 6.3%-18.3%, Palestine shows a higher rate of 24%, Japan and Taiwan around 13%-15%(9). Unlike the case with East Asia, the prevalence of GERD ranges from 2% - 8% (9). In Indonesia, there is no definite epidemiological data on the prevalence of GERD, however, at Cipto Mangunkusumo Hospital, Jakarta, 22.8% of esophagitis cases were found in all patients undergoing endoscopy for indications of dyspepsia(10). The diagnosis of GERD according to the national GERD consensus in Indonesia can use several tools such as GERD-Q, upper gastrointestinal endoscopy, PPI test and 24-hour pH meter test(20).

Until now, the actual relationship between H. Pylori and GERD is still unclear because some studies report a high prevalence of H. Pylori in GERD patients, but some studies report the opposite (5). Further research is necessary to clarify this relationship. This study was conducted to determine the relationship between H. pylori infection and GERD and the prevalence of H. Pylori infection among patients with GERD at Eka Hospital Pekanbaru.

METHOD

A cross-sectional study was conducted on 219 patients who were selected consecutively from candidates who had a diagnosis of GERD during upper digestive tract endoscopy (gastroscopy) for almost two years (January 2021 - December 2022) at Eka Hospital Pekanbaru. All patients over 18 years who were diagnosed with GERD based on clinical symptoms, such as burning sensation in the chest or regurgitation that occurs after eating and did not respond to PPI therapy for 2 weeks, were included in this study.. Diagnosis of H. Pylori is based on anatomic pathological examination of the gastric biopsy during endoscopy. Patients who had abnormal esophageal endoscopy other than GERD, such as malignancy or history of gastric surgery, were excluded from the study. In this study, we evaluated the relationship between H. Pylori infection and GERD, as well as the prevalence of H. Pylori infection in patients diagnosed with GERD.

Demographic data (age, gender, weight) are discussed along with the endoscopic appearance of the esophageal mucosa in patients with positive H. Pylori compared to those with negative H. Pylori. Analyzing using the Chi-square test with SPSS version 22.

RESULT

Table 1 shows that 219 patients who were diagnosed with GERD and underwent endoscopy had an average age of 45 years, with a predominance of <60 years (183 patients) and more in women (118 patients). Based on endoscopy results, this study found a prevalence of 49.3%.

Table 1. Characteristic Data (N = 219)

Variable	f (%)
Age	
Mean	45,79 ± 13,928
Min	17 years
Max	78 years
Age	
≥ 60 years	36 (16,4 %)
< 60 years	183 (83,6 %)
Sex	
Man	101 (46,1 %)
Women	118 (53,9 %)
Infeksi Helicobacter pylori (HP)	
Positive	108 (49,3 %)
Negative	111 (50,7 %)

Table 2. Shows the relationship between H. Pylori infection and GERD based on the patient's age. The age group was divided into ≥60 years and <60 years. Based on the analysis test, it was found that GERD patients aged ≥60 years had H. Pylori infection (positive) in 14 patients (13%), while in patients <60 years who had H. Pylori infection (positive) there were 94 patients (87%). The statistical results show that age ≥60 years in GERD patients have a lower risk factor for H. Pylori infection than age <60 years as indicated by an RR value of 0.063 (less than 1), with a 95% confidence interval within the prevalence ratio range of 0.290- 1,250. However, this result was not statistically significant with a value of p = 0.418 (p > 0.05).

Table 2. Helicobacter Pylori (HP) infection in GERD patients based on patient age

Variable	Helicobacter pylori				RR	CI 95%	p
	infection (HP)						
	Positive		Negative				
	n	%	n	%			
Age							
≥ 60 years	14	13	22	19,8	0,063	0,290-1,250	0,203
< 60 years	94	87	89	80,2			

p = probability value

* p value < 0,05 = statistically significant difference

Table 3. *Helicobacter Pylori* (HP) infection in GERD patients based on gender

Variable	Helicobacter pylori infection (HP)				RR	CI 95%	p
	Positive		Negative				
	n	%	n	%			
Sex							
Man	53	49,1	48	43,2	1,265	0,743-2,154	0,418
Women	55	50,9	63	56,8			

p = probability value

* p value < 0,05 = statistically significant difference

Table 3. Shows the relationship between H. Pylori infection and GERD based on gender. GERD patients infected with H. Pylori were more common in women, namely 55 patients (50.9%) while men were 53 patients (49.1%). The statistical results show that the female gender in GERD patients has a higher risk of H. Pylori infection than the male as indicated by the RR value of 1.265 (more than 1), and the prevalence ratio lies between 0.743-2.154 with a 95% confidence interval. However, these results were not statistically significant with a value of $p = 0.418$ ($p > 0.05$).

Table 4. *Helicobacter Pylori* (HP) infection in GERD patients based on anatomical pathology

Variable	Helicobacter pylori infection (HP)				p
	Positive		Negative		
	N	%	n	%	
Anatomical Pathology					
Chronic Gastritis	33	15,1	46	21,0	0,377
Erosive chronic gastritis	35	16,0	29	13,2	
Chronic gastritis with atrophy	24	11,0	24	11,0	
Chronic gastritis with atrophy and metaplasia	11	5,0	6	2,7	
Gaster ulcer	5	2,3	6	2,7	

p = probability value

* p value < 0,05 = statistically significant difference

In Table 4. Shows the relationship between H. Pylori infection and GERD based on the anatomical pathology (PA). The results of anatomical pathology (PA) in endoscopes GERD patients showed chronic gastritis in 33 patients, chronic erosive gastritis in 35 patients, chronic gastritis with atrophy in 24 patients, chronic gastritis with atrophy and metaplasia in 11 patients and the presence of gastric ulcers in 5 patients. On examination of anatomical pathology in patients with GERD, there was no significant difference ($p > 0.05$; $p = 0.377$) for those who had H. Pylori infection (positive) compared to those who did not have H. Pylori infection (negative). Erosive chronic gastritis is the most common anatomic pathological finding found in GERD patients in this study.

DISCUSSION

In this study, the prevalence of GERD patients who were infected with H. Pylori in almost two years at Eka hospital was 49.3% (108) H. Pylori positive patients out of 219 GERD patients. The prevalence of GERD symptoms reported at least weekly in population-based studies worldwide is approximately 13%, although there is significant geographic variation(11). Research in Indonesia found prevalence variations between 5.7-68% due to differences in ethnicity and geographical areas in Indonesia(4). Some habits can significantly increase the prevalence of H. Pylori, such as eating food with fingers, rarely washing hands before eating, eating cucumber more than once a week and drinking alcohol, salary, source of water, type of latrines, a history of taking medication, religion, and smoking(4). A study in 2014 identified and reported a GERD prevalence of 10-20% in Europe and the United States, but less than 5% in Asia(12). Systematic reviews, found a symptom-based prevalence of GERD in East Asia of 2.5–4.8% before 2005 and 5.2–8.5% between 2005 and 2010 (based on population-based studies)(13). The prevalence was found to be higher in Southeast and West Asia (6.3-18.3% after 2005)(13).

In a study conducted in Iran involving 1916 GERD patients, age, BMI and smoking significantly increased H. Pylori infection compared to patients without GERD, and found no significant differences in terms of gender, socio-demographic status and ethnicity(3). In an Israeli study involving 2500 GERD patients, the prevalence of H. pylori infection among patients with symptoms suggestive of GERD was approximately 12%(14). In some studies, H. Pylori infection was not associated with GERD, but there is no strong evidence of a lower prevalence of H. Pylori infection in patients with GERD and this so-called “protective” effect(3).

Some studies have reported a higher prevalence of H. Pylori infection in patients with GERD, while some studies have observed an inverse relationship(5). This relationship is difficult to justify because GERD is a disease that is influenced by various risk factors such as BMI, smoking, lifestyle habits and others(5). A collaborative study between South Asian countries reported that host genetic susceptibility, H. pylori genetic diversity and environmental factors were associated with H. Pylori infection(4). Several habits can increase the prevalence of H. Pylori significantly, such as eating food with fingers, rarely washing hands before eating, eating cucumber more than once a week and drinking alcohol(4). H. Pylori can usually be transmitted directly and indirectly(15). Direct

transmission involves intimate interactions such as kissing an open mouth or sharing cutlery/cups, while indirect transmission requires media such as air, drinking water, food, flies or other animals(15). The most widespread spread of H. Pylori is via the oral-oral or faecal-oral route(2). The main risk factors remain related to socio-economic, family living conditions and environmental factors such as lack of proper sanitation, proper drinking water and hygiene, as well as unsanitary food and overcrowding, all of which determine the prevalence of this infection(2).

In this study, it was found that the number of female patients (50.9%) was slightly more than male (49.1%) infected with H. Pylori. In addition, from this study it was found that women are more at risk of H. Pylori infection than men, although this is not statistically significant. In a study conducted in Yemen, there was no gender difference between males and females in patients infected with H. Pylori(16). Gender is also not dominant towards men or women, but the frequency of occurrence is higher in men (25.8%) than women (18.9%)(17). A Chinese study showed that the prevalence of H. Pylori infection was higher in women than men (49.2% vs. 47.9%, $p = 0.002$), possibly because women had higher levels of IL-35 than men among ulcer patients, H. Pylori-infected stomach, H. Pylori-infected asymptomatic subjects, and uninfected healthy individuals and failure of H. Pylori eradication in chronic gastritis(15).

In this study, it was found that there were more GERD patients aged <60 years (87%) than ≥60 years (13%). In addition, age <60 years are more at risk of being positive for H. Pylori than age ≥60 years, although this study is not statistically significant. In a Chinese study, it was found that H. Pylori infection increased with age, peaking in the 51–60 years age group and in a multivariate analysis, age was also found to be a significant predictor of H. Pylori infection(19). The host immune response to H. Pylori is very complex and can change depending on age, where during childhood the predominant pattern of inflammation (Treg), with higher concentrations of TGF-β1 and IL-10, makes the gastric mucosa of children more vulnerable. Against H. Pylori colonization(16). In adults the dominant Th1 response, with higher levels of IFN-γ and IL-12p70 in the gastric mucosa thereby inducing excessive inflammatory activity and causing a greater risk of gastric damage(18).

In this study, the dominant histological features in positive H. Pylori were 16% erosive chronic gastritis and 11% chronic gastritis accompanied by atrophy,

5% chronic gastritis with atrophy and metaplasia. A gastritis that lasts a long time can cause atrophy of the gastric mucosa, then the atrophic part will be replaced by metaplastic glands so that intestinal metaplasia can occur(17). H. Pylori according to WHO is categorized as a type 1 carcinogen so that H. Pylori infection is the strongest risk factor for the development of stomach cancer, and many studies have supported this relationship(21). H. Pylori infection leads to the development of chronic atrophic gastritis with intestinal dysplasia, which significantly increases the risk of gastric cancer(21).

The lack of consideration of factors like lifestyle, smoking, diet, BMI, socioeconomic status, ethnicity, and neighborhood is a weakness of this study. Given the high prevalence of patients with GERD and H. Pylori in this study (49.5%), it would be advantageous if every patient diagnosed with GERD and treated with PPI for 8 weeks, but without any improvement, could be screened for H. Pylori infection through endoscopic examination. The relationship between GERD and H. Pylori needs to be established by further research that considers the above risk factors.

CONCLUSION

Although the prevalence of GERD patients infected with H. pylori was quite high (49.3%), there was no significant association between GERD patients and H. Pylori infection.

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